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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,936	11/07/2001	Olle Korsgren	KORSGREN-1	9165

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WASHINGTON, DC 20001-5303

EXAMINER

JAGOE, DONNA A

ART UNIT	PAPER NUMBER
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1614

MAIL DATE	DELIVERY MODE
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08/09/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/890,936

Applicant(s)

KORSGREN ET AL.

Examiner

Donna Jagoe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4,8,9,11 and 14-26 is/are pending in the application.
- 4a) Of the above claim(s) 14-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4,8,9 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. <u>6/28/07</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 4, 8, 9, 11 and 14-26 are pending in this application. Claims 14-26 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 8, 9 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In particular, "individually isolated islets to a patient suffering from insulin dependent diabetes mellitus (IDDM), wherein said individually isolated islets are modified by irreversible adsorption with a clotting inhibiting agent comprising heparin or a fraction or derivative thereof, wherein said individual islets cells are each separately coated with heparin" (present claim 1) is a concept that was not present in the specification as originally filed. The Examiner contends that such "individually separately coated islets cells" was not present in the specification as originally filed.

Written Description

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An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The Examiner is guided in his opinion that Applicant has not adequately described the presently claimed subject matter by the MPEP at § 2163 - 2163.05. In particular, while Applicant's specification as originally filed contained a teaching of using a conjugate of heparin to coat the islets (see page 3 if instant specification), but does not contain a teaching of "individually isolated" and "individually coated" islets cells.

Considering the teachings provided in the specification as originally filed, the Examiner finds that Applicants have failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicants had possession of the concept of an "individually isolated islets cell" and an "individually coated islet cell".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 4, 8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al. DE 196 23 440 A 1.

Wagner et al. teach method of use of anticoagulants such as heparin, hirudin and Marcumar and derivatives thereof in connection with transplantation of insulin producing cells such as islets of Langerhans (see claim 8). The cells may be in the form of microencapsulated islets (see figure 1 and claim 10) and where immunosuppression can be an issue, see "Islet Transplant Info" that teaches that immunosuppression and/or appropriate drugs, such as Zenapax should be used to address the issue. The abstract for Wagner et al. teach that the immobilized material is insulin, proinsulin and/or organ cells of xenogenic or autogenic origin (islets of Langerhans, etc.) and the system contains an agent to inhibit or suppress blood agglutination, agglomeration antagonists, heparin, hirudin, marcumar and their derivatives. Wagner discloses that the islets *may* be microencapsulated. Additionally, if the cells are microencapsulated, they are first mixed with the anticoagulant material, thus anticipated the claims of the instant application.

Claims 4, 8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Soon-Shiong et al. U.S. 5,705,270 A.

Soon-Shiong et al. teach microcapsules containing biological material such as islet of Langerhans cells coated with polymerizable materials (see abstract, see also claim 3). The microcapsules are covalently linked with heparin (see claim 5). Soon-Shiong et al. teach encapsulation of islets of Langerhans for treatment of diabetes (column 4, lines 1-4) to prevent the detrimental effects of capsule instability on the

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encapsulated biologically active material e.g. loss of immunoprotection for the encapsulated material is minimized (column 3, lines 61-66). Additionally, note that there is no provision in the instant claims that deals with the immunosuppression issue, without which, the transplanted islet cells would be rejected (see Islet Transplant Info). The instant specification describes immobilizing heparin according to a method developed by Corline Systems AB disclosed in WO 93/05793 (page 4 of the instant specification). The heparin in WO 93/05793 appears to be immobilized (conjugated) with a polymer comprising a substantially straight-chained organic homo or hetero polymer having a number of functional groups distributed along the polymer backbone chain via which groups at least about 20 molecules (see page 7 of WO 93/05793). While applicant asserts that the heparin is not in microcapsules, it appears that it is similarly coated and as such, must form micro (or macro) capsules if applicant has followed the technique of Corline Systems AB as recited in applicants specification.

Claims 4, 8, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nomura et al. (AG from IDS dated 11/17/03).

Nomura et al. teach islet transplantation for the treatment of type I diabetes after the islets cells were collected and administered with various doses of heparin (page 1849, column 1, paragraph 3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 9 rejected under 35 U.S.C. 103(a) as being unpatentable over Soon-Shiong et al. U.S. 5,705,270 A and Wagner et al. DE 196 23 440 A 1 as applied to claims 4, 8 and 11 above, and further in view of Couser et al. 1995.

Couser et al. teach that complement is a major mediator of tissue injury in several types of glomerulonephritis (see abstract) and that an inhibitor of complement

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activation, sCR1 has shown beneficial effects on several forms of tissue injury including xenograft transplantation (page 1892, column 1, 1st full paragraph).

Soon-Shiong et al. teach microcapsules containing biological material such as islet of Langerhans cells coated with polymerizable materials (see abstract, see also claim 3). The microcapsules are covalently linked with heparin (see claim 5). Soon-Shiong et al. teach encapsulation of islets of Langerhans for treatment of diabetes (column 4, lines 1-4) to prevent the detrimental effects of capsule instability on the encapsulated biologically active material e.g. loss of immunoprotection for the encapsulated material is minimized (column 3, lines 61-66). Wagner et al. teach method of use of anticoagulants such as heparin, hirudin and Marcumar and derivatives thereof in connection with transplantation of insulin producing cells such as islets of Langerhans (see claim 8). Davis teaches that the formation of complement is a problem and results in HAR during xenotransplantation.

One of ordinary skill in the art would have administered an inhibitor of complement formation such as sCR1 during islet transplantation since it was well known in the art at the time the invention was made that the formation of complement results in tissue injury and that Couser et al. teach that an inhibitor of complement activation, sCR1 has shown beneficial effects on several forms of tissue injury including xenograft transplantation (page 1892, column 1, 1st full paragraph).

Response to Arguments

Applicant's arguments filed April 4, 2007 have been fully considered but they are not persuasive.

Applicant asserts that there is nothing in either Wagner or Soon-Shiong which has anything to do with irreversible adsorption. In response, although these words are not used, the islet cells are combined with heparin and encapsulated with a polymer such as alginate. Wagner discloses that the islets may be microencapsulated. Additionally, if the cells are microencapsulated, they are first mixed with the anticoagulant material, thus anticipated the claims of the instant application. Soon-Shiong et al. teach microcapsules containing biological material such as islet of Langerhans cells coated with polymerizable materials (see abstract, see also claim 3). The microcapsules are covalently linked with heparin (see claim 5). Bennet et al. teach transplantation of isolated islets of Langerhans with heparin and optionally the complement inhibitor sCR-1. The instant specification describes immobilizing heparin according to a method developed by Corline Systems AB disclosed in WO 93/05793 (page 4 of the instant specification). The heparin in WO 93/05793 appears to be immobilized (conjugated) with a polymer comprising a substantially straight-chained organic homo or hetero polymer having a number of functional groups distributed along the polymer backbone chain via which groups at least about 20 molecules (see page 7 of WO 93/05793). While applicant asserts that the heparin is not in microcapsules, it appears that it is similarly coated and as such, must form micro (or macro) capsules if applicant has followed the technique of Corline Systems AB as recited in applicants

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specification. Claims are not construed in a vacuum, but rather in the context of the intrinsic evidence, viz, the other claims, the specification and the prosecution history. Applicants argument regarding the "dead space" used by Novocel Inc, for example is not well taken. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., dead space in a prior art reference) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Regarding the reference to the affidavit showing close contact and no "dead space", the comparative showing did not provide an adequate basis to support a legal conclusion of non-anticipation. Regarding the puzzling argument in the final office action, it was in response to an assertion made that the Corline System refers to "tubing used as a tool for testing modified islets and has no function whatsoever to encapsulate any islets" (see page 5 of the reply to office action dated June 21, 2006).

Interview Summary

Applicant has indicated that a copy of the interview summary dated June 28, 2007 has not been received. Enclosed is a copy of said interview summary.

Correspondence

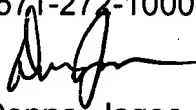
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-

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0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Donna Jagoe
Patent Examiner
Art Unit 1614

August 6, 2007